

Clinical, electroencephalographic and magnetic resonance imaging characteristics of epilepsy associated with cerebral cavernous malformation

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ABSTRACT

Objectives: To describe the clinical, electroencephalographic (EEG) and magnetic resonance imaging (MRI) characteristics of patients with epilepsy associated with cerebral cavernous malformation (CCM), and to determine the association between MRI features and EEG abnormalities.

Methods: A retrospective cross-sectional study of the medical records of 63 consecutive patients treated at Bach Mai National Institute of Neuroscience from January 2025 to August 2026. Associations were tested with the chi-square or Fisher's exact test.

Results: The mean age was 42.9 ± 14.9 years; 60.3% of patients were male. Focal-onset seizures accounted for 68.3%, most commonly focal to bilateral tonic-clonic seizures (36.5%). EEG was abnormal in 42.9% of patients (epileptiform discharges, 31.7%). Lesions were mainly frontal (42.9%) and temporal (34.9%), and 77.8% of patients had a single lesion. EEG abnormality was associated with lesion lobe ($p=0.024$) and relation to the cortex ($p=0.023$), and was most frequent with cortical lesions (75.0%). Patients aged ≤ 40 years had more EEG abnormalities (57.6% vs. 26.7%; $p=0.013$) and more cortical lesions (30.3% vs. 6.7%; $p=0.002$) than older patients.

Conclusion: In CCM-related epilepsy, focal-onset seizures predominate, and routine EEG abnormalities are associated with lesion location, particularly cortical involvement.

Keywords: epilepsy, cerebral cavernous malformation, electroencephalography, brain magnetic resonance imaging.

1. INTRODUCTION

Cerebral cavernous malformation (CCM) is a vascular malformation of the brain composed of dilated, thin-walled vascular spaces without intervening neural tissue. These lesions may be single

or multiple and are typically detected on brain magnetic resonance imaging (MRI).¹ The clinical presentation of CCM ranges from asymptomatic lesions to headache, intracerebral hemorrhage, focal neurological deficits and epilepsy. Epilepsy is one of the most common manifestations and is particularly associated with cortical lesions.² Electroencephalography (EEG) is an important tool for detecting abnormal brain electrical activity, helping to localize the epileptogenic zone and classify seizure types.³ Brain MRI is the primary modality for detecting and evaluating CCM, and susceptibility-weighted sequences are highly sensitive to hemosiderin, old hemorrhage and small or multiple lesions.⁴

The reported clinical, EEG and MRI characteristics of CCM-related epilepsy vary across studies. In Vietnam, published data on CCM are limited and have mainly addressed hemorrhage and its risk factors,⁵ whereas data on the EEG and MRI features of CCM-related epilepsy remain scarce. This study therefore aimed (1) to describe the clinical, EEG and MRI characteristics of patients with epilepsy associated with CCM, and (2) to determine the association between MRI features and EEG abnormalities, including differences between age groups.

II. SUBJECTS AND METHODS

2.1. Study subjects

The study used the medical records of inpatients and outpatients with epilepsy associated with CCM who were treated at Bach Mai National Institute of Neuroscience, Bach Mai Hospital, Hanoi, Vietnam, from January 2025 to August 2026.

Inclusion criteria: medical records of patients with (1) epilepsy diagnosed according to the 2017 International League Against Epilepsy (ILAE) definitions and classification; (2) brain MRI showing CCM; (3) a routine EEG recorded at Bach

Mai National Institute of Neuroscience; and (4) sufficient clinical, EEG and MRI data for analysis.

Exclusion criteria: records of patients who had only acute symptomatic seizures (seizures occurring with an acute metabolic disturbance such as hypoglycemia, hyperglycemia, hyponatremia or metabolic acidosis, or only within 7 days of an acute hemorrhage from the CCM).

2.2. Study methods

Study design: Cross-sectional descriptive study based on a retrospective review of medical records.

Sample size and sampling: Total consecutive sampling was used: the records of all consecutive patients who met the inclusion criteria and none of the exclusion criteria during the study period were enrolled; no formal sample size calculation was performed because CCM-related epilepsy is uncommon. The final sample comprised 63 patients.

MRI: Brain MRI was performed on a Philips Ingenia Prodiva 1.5T CX system (Bach Mai Hospital) with T1-weighted, T2-weighted, FLAIR, diffusion-weighted and susceptibility-sensitive (SWI or T2*-GRE) sequences. CCM was diagnosed on the typical appearance of a lesion with a mixed-signal core and a hypointense hemosiderin rim, as reported by radiologists at Bach Mai Hospital; MRI performed elsewhere was accepted only after review by radiologists of the Bach Mai Radiology Center. MRI variables were extracted from the full radiology reports. Lesion location by lobe was classified as frontal, temporal or parietal lobe, regardless of side (patients whose lesions were all within the same lobe, including bilateral lesions in that lobe, were assigned to that lobe); "multiple locations" (lesions in two or more lobes or regions); or "other region" (a single lesion outside the cerebral lobes, such as the cingulate gyrus, corpus callosum or basal ganglia). Location relative to the cortex was classified as cortical (lesion within or in contact with the cortex),

subcortical (in the white matter beneath the cortex without cortical contact), deep (in deep structures such as the basal ganglia, thalamus, corpus callosum or brainstem) or mixed (lesions in more than one of these compartments). Lesion size was the maximum diameter (mm), grouped a priori as <10 mm, 10–<20 mm and ≥20 mm. For patients with multiple lesions, lesion size and signs of hemorrhage were recorded for the lesion considered responsible for the seizures (concordant with seizure semiology and/or EEG) or, if this could not be determined, for the largest lesion.

EEG: Routine interictal scalp EEG was recorded on a Nihon Kohden system at the EEG laboratory of Bach Mai National Institute of Neuroscience, following the procedure of the Ministry of Health. Electrodes were placed according to the international 10–20 system, and recordings lasted 20–30 minutes with eye opening–closing, hyperventilation and intermittent photic stimulation.³ Recordings were interpreted by neurologists. EEG was classified as normal or abnormal; abnormal EEG included (a) epileptiform discharges (spikes, sharp waves, spike-wave or sharp-slow-wave complexes, polyspikes) and (b) slow-wave activity only (focal or diffuse theta/delta activity without epileptiform discharges).

Variables: age, sex; seizure type according to the ILAE 2017 classification; EEG findings; and MRI characteristics (lesion location by lobe, number of lesions, location relative to the cortex, lesion size and signs of hemorrhage). For comparisons, patients were divided into two age groups (≤40 and >40 years) using the median age of the sample (40 years) as the cut-off.

Statistical analysis: Data were analysed with IBM SPSS Statistics 26.0. Quantitative variables were presented as mean ± standard deviation (SD) or median (interquartile range) according to their

distribution, and categorical variables as frequency and percentage. Proportions were compared with the chi-square (χ^2) test; Fisher's exact test (2×2 tables) or the Fisher–Freeman–Halton exact test (larger tables) was used when more than 20% of cells had an expected count <5. A two-sided $p<0.05$ was considered statistically significant.

2.3. Research ethics

The study was approved by the Biomedical Research Ethics Committee of Bach Mai Hospital (IRB-VN01019) under Approval Certificate No. 394/BM-HĐĐĐ dated 8 July 2026 (dossier code IRB-BMH-ĐT.RG-2026.09.Đ12). This was an observational study based on a retrospective review of medical records, without any intervention; data were extracted in accordance with the approval and the regulations of Bach Mai Hospital. All data were coded and anonymised, and results are reported only in aggregate form.

III. RESULTS

A total of 63 patients with epilepsy associated with CCM were included; their general characteristics are shown in Table 1.

Table 1. General characteristics of participants (n=63)

Characteristic	Subgroup	n	%
Age group (years)	<20	5	7.9
	20-30	7	11.1
	31-40	21	33.3
	41-50	10	15.9
	51-60	9	14.3
	>60	11	17.5
Age (years)	Mean ± SD (range)	42.9 ± 14.9 (15-78)	
Age group for comparison	≤40 years	33	52.4
	>40 years	30	47.6
Sex	Male	38	60.3
	Female	25	39.7

The mean age was 42.9 ± 14.9 years (range 15–78 years). The 31–40-year group accounted for the highest proportion (33.3%), followed by patients older than 60 years (17.5%) and those aged 41–50 years (15.9%), whereas patients younger than 20 years accounted for the lowest proportion (7.9%). Patients aged ≤ 40 years and >40 years accounted for 52.4% and 47.6%, respectively. Males predominated (38/63; 60.3%), with a male-to-female ratio of approximately 1.5:1.

Table 2. Clinical seizure characteristics of participants (n=63)

Seizure onset	Seizure type	n	%
Focal onset (n=43, 68.3%)	Focal aware seizure	3	4.8
	Focal impaired-awareness seizure	17	27.0
	Focal to bilateral tonic-clonic seizure	23	36.5
Generalized onset	Generalized-onset seizure	18	28.6
Unknown onset	Unknown-onset seizure	2	3.2
Total		63	100.0

Focal-onset seizures predominated (43/63; 68.3%), with focal to bilateral tonic-clonic seizures accounting for the highest proportion (36.5%), followed by focal impaired-awareness seizures (27.0%). Generalized-onset seizures accounted for 28.6% (Table 2).

Table 3. EEG characteristics of participants (n=63)

EEG finding		n	%
Normal		36	57.1
Abnormal		27	42.9
	Slow-wave activity only	7	11.1
	Epileptiform discharges	20	31.7
Total		63	100.0

As shown in Table 3, EEG was abnormal in 27 patients (42.9%): 20 (31.7%) had epileptiform discharges and 7 (11.1%) had slow-wave activity only. EEG was normal in 36 patients (57.1%).

Table 4. MRI characteristics of cavernous malformations (n=63)

Characteristic	Subgroup	n	%
Location by lobe	Frontal lobe	27	42.9
	Temporal lobe	22	34.9
	Parietal lobe	2	3.2
	Multiple locations	9	14.3
	Other region	3	4.8
Number of lesions	Single	49	77.8
	Multiple	14	22.2
Location relative to cortex	Cortical	12	19.0
	Subcortical	23	36.5
	Deep	18	28.6
	Mixed	10	15.9
Lesion size	<10 mm	18	28.6
	10–<20 mm	37	58.7
	≥ 20 mm	8	12.7
	Median (IQR), mm	13.0 (9.0–17.0)	
Signs of hemorrhage	Present	11	17.5

The frontal lobe was the most common location (42.9%), followed by the temporal lobe (34.9%); lesions in multiple locations and in other regions accounted for 14.3% and 4.8%, respectively, and the parietal lobe was the least common (3.2%). Most patients had a single lesion (77.8%) measuring <20 mm (87.3%; median 13.0 mm). Subcortical (36.5%) and deep (28.6%) lesions were more frequent than cortical (19.0%) and mixed (15.9%) lesions (Table 4).

Table 5. Association between MRI characteristics (lesion location by lobe, number of lesions, location relative to the cortex, size, hemorrhage) and abnormal EEG

Characteristic	Subgroup	Abnormal EEG n (%)	Normal EEG n (%)	p
Location by lobe	Frontal lobe	16 (59.3)	11 (40.7)	0.024**
	Temporal lobe	4 (18.2)	18 (81.8)	
	Parietal lobe	1 (50.0)	1 (50.0)	
	Other region	1 (33.3)	2 (66.7)	
	Multiple locations	5 (55.6)	4 (44.4)	
Number of lesions	Single	20 (40.8)	29 (59.2)	0.540*
	Multiple	7 (50.0)	7 (50.0)	
Location relative to cortex	Cortical	9 (75.0)	3 (25.0)	0.023*
	Subcortical	6 (26.1)	17 (73.9)	
	Deep	6 (33.3)	12 (66.7)	
	Mixed	6 (60.0)	4 (40.0)	
Lesion size	<10 mm	4 (22.2)	14 (77.8)	0.094**
	10–<20 mm	19 (51.4)	18 (48.6)	
	≥20 mm	4 (50.0)	4 (50.0)	
Signs of hemorrhage	Present	5 (45.5)	6 (54.5)	1.000**
	Absent	22 (42.3)	30 (57.7)	

Abnormal EEG: epileptiform discharges or slow-wave activity only. Percentages are row percentages.

* Chi-square test (χ^2); ** Fisher's exact test (Fisher-Freeman-Halton test for tables larger than 2×2).

Lesion location by lobe was significantly associated with abnormal EEG ($p=0.024$): the abnormality rate was highest with frontal lesions (59.3%) and lowest with temporal lesions (18.2%). Location relative to the cortex was also associated with abnormal EEG ($p=0.023$), with the highest rate for cortical lesions (75.0%) and lower rates for subcortical (26.1%) and deep (33.3%) lesions. The number of lesions ($p=0.540$), lesion size ($p=0.094$) and signs of hemorrhage ($p=1.000$) were not significantly associated with abnormal EEG (Table 5).

Table 6. Clinical, MRI and EEG characteristics in patients aged ≤40 years versus >40 years

Characteristic	Subgroup	≤40 years (n=33) n (%)	>40 years (n=30) n (%)	p
Seizure onset	Focal	24 (72.7)	19 (63.3)	0.785**
	Generalized	8 (24.2)	10 (33.3)	
	Unknown	1 (3.0)	1 (3.3)	
EEG	Abnormal	19 (57.6)	8 (26.7)	0.013*
	Normal	14 (42.4)	22 (73.3)	

Characteristic	Subgroup	≤40 years (n=33) n (%)	>40 years (n=30) n (%)	p
Location relative to cortex	Cortical	10 (30.3)	2 (6.7)	0.002*
	Subcortical	11 (33.3)	12 (40.0)	
	Deep	4 (12.1)	14 (46.7)	
	Mixed	8 (24.2)	2 (6.7)	
Number of lesions	Single	23 (69.7)	26 (86.7)	0.106*
	Multiple	10 (30.3)	4 (13.3)	
Lesion size	<10 mm	8 (24.2)	10 (33.3)	0.394**
	10-<20 mm	19 (57.6)	18 (60.0)	
	≥20 mm	6 (18.2)	2 (6.7)	

Percentages are column percentages. * Chi-square test (χ^2); ** Fisher-Freeman-Halton exact test.

Table 6 shows that patients aged ≤40 years had a significantly higher rate of abnormal EEG than those aged >40 years (57.6% vs. 26.7%; $p=0.013$). Location relative to the cortex also differed between the groups ($p=0.002$): cortical (30.3% vs. 6.7%) and mixed (24.2% vs. 6.7%) lesions were more frequent in the younger group, whereas deep lesions were more frequent in the older group (46.7% vs. 12.1%). There were no significant differences in seizure onset ($p=0.785$), number of lesions ($p=0.106$) or lesion size ($p=0.394$).

IV DISCUSSION

The mean age of our patients was 42.9 ± 14.9 years, and most were young or middle-aged adults (Table 1). Zhang et al. found that an age at diagnosis ≤44 years was associated with a higher risk of epilepsy among patients with CCM (OR [odds ratio]=2.79; $p=0.010$).² Because our study included only patients with epilepsy and had no comparison group without epilepsy, our data cannot test this association; however, the age distribution of our sample is in line with this observation. Our patients were older than those in surgical series of CCM-related epilepsy, such as the study by Nico et al. (mean age 36.1 ±

14.6 years),⁶ probably because surgical cohorts select younger patients with drug-resistant epilepsy. Notably, 17.5% of our patients were older than 60 years, suggesting that CCM should also be considered as a structural cause in elderly patients presenting with seizures.

Males accounted for 60.3% of our patients, similar to the proportion reported by Nico et al. (58.7%),⁶ whereas Nguyễn Huệ Linh and Võ Hồng Khôi reported a similar proportion of men and women among patients with CCM at Bach Mai Hospital.⁵ As our study had no comparison group, the male predominance more likely reflects the characteristics of this hospital-based sample than a sex-specific risk.

Focal-onset seizures predominated (68.3%), and focal to bilateral tonic-clonic seizures were the most common type (36.5%), followed by focal impaired-awareness seizures (27.0%). This is consistent with the study by Zhang et al., in which focal to bilateral tonic-clonic seizures were the most common seizure type in CCM-related epilepsy.² The relatively high proportion of generalized-onset seizures (28.6%) may partly reflect classification based mainly on the history recorded in medical records, as a brief focal phase may be missed when seizures occur during sleep or without a witness.

Routine EEG was abnormal in 42.9% of

patients, with epileptiform discharges in 31.7% and normal recordings in 57.1%. In a population-based study of 520 adults with a first unprovoked seizure, Joelsson et al. found epileptiform discharges on the first EEG in only 7.7% of patients, with a median interval of 70 days from seizure to EEG, and a shorter interval was associated with a higher yield.⁷ The higher rate in our study may be explained by the structural aetiology of all patients and by the fact that about half of the recordings (50.8%) were obtained within 72 hours after the most recent seizure. Conversely, a normal routine EEG does not exclude epilepsy, as interictal discharges may not occur during a short recording, and deep or medially located lesions may produce scalp EEG findings that do not correspond to the lesion location on MRI.⁸

On MRI, frontal lobe lesions were the most common (42.9%), followed by temporal lobe lesions (34.9%). This distribution is similar to that reported by Nico et al. in patients with CCM-related epilepsy (frontal 40%, temporal 35%),⁶ and the frontal lobe was also the most frequent location in the Vietnamese study by Nguyen Hue Linh and Vo Hong Khoi.⁵ Most patients had a single lesion smaller than 20 mm, and subcortical and deep lesions were more frequent than purely cortical lesions.

A notable finding of this study was the association between lesion location and abnormal EEG. Lesion location by lobe was significantly associated with EEG abnormality ($p=0.024$), with the highest rate in frontal lesions (59.3%) and the lowest in temporal lesions (18.2%). The low rate in temporal lesions may relate to the limited sensitivity of scalp EEG for mesial temporal sources. In addition, cortical lesions had the highest rate of abnormal EEG (75.0%; $p=0.023$). This is consistent with reports that the risk of epilepsy in CCM is closely related to cortical involvement.^{2,4} Proposed

mechanisms include recurrent microhemorrhage, hemosiderin deposition, neuroinflammation and changes in the perilesional microenvironment, which affect the excitability of adjacent cortical neurons.^{1,9} However, given the small numbers in several subgroups, these associations should be interpreted with caution.

In contrast, the number of lesions was not significantly associated with abnormal EEG ($p=0.540$); the abnormality rate in patients with multiple lesions (50.0%) was only slightly higher than in those with a single lesion (40.8%). Lesion size and signs of hemorrhage were also not associated with abnormal EEG. These findings suggest that, in our sample, lesion location and cortical involvement were more closely related to EEG abnormality than lesion number or size.

By age group, there were no significant differences in seizure onset, number of lesions or lesion size between patients aged ≤ 40 and >40 years. However, the younger group had a significantly higher rate of abnormal EEG (57.6% vs. 26.7%; $p=0.013$) and a higher proportion of cortical lesions (30.3% vs. 6.7%), whereas the older group had more deep lesions (46.7% vs. 12.1%; $p=0.002$). Because cortical lesions were associated with EEG abnormality, the difference in EEG findings between age groups may partly reflect the different distribution of lesion location; this hypothesis could not be tested in our study and requires confirmation in larger samples with multivariable analysis.

This study provides clinical, EEG and MRI data on CCM-related epilepsy in Vietnam, particularly on the relationship between lesion location and EEG abnormality. The study has several limitations. First, it was a retrospective, single-centre study with total consecutive hospital-based sampling; data depended on the completeness of medical records, and generalisability may be limited. Second, the sample size was small, and several subgroups had low cell counts, reducing statistical

power. Third, there was no control group of patients with CCM without epilepsy, so risk factors for epilepsy could not be assessed. Fourth, only a single routine interictal EEG was analysed, without sleep or prolonged video-EEG recording, and MRI features were obtained from routine radiology reports without standardised re-reading.

V CONCLUSION

Epilepsy associated with cerebral cavernous malformation in this study mainly occurred in young and middle-aged adults (mean age 42.9 ± 14.9 years). Focal-onset seizures predominated (68.3%), especially focal to bilateral tonic-clonic seizures (36.5%) and focal impaired-awareness seizures (27.0%). Routine EEG was abnormal in 42.9% of patients, with epileptiform discharges in 31.7%. On MRI, frontal (42.9%) and temporal (34.9%) lesions predominated, and most patients had a single lesion (77.8%) smaller than 20 mm (87.3%). Lesion location by lobe and relation to the cortex were associated with abnormal EEG ($p=0.024$ and $p=0.023$), with the highest rate of EEG abnormality in cortical lesions (75.0%). Compared with patients aged >40 years, patients aged ≤ 40 years had a higher rate of abnormal EEG ($p=0.013$) and more cortical lesions ($p=0.002$), whereas seizure onset, number of lesions and lesion size did not differ between age groups.

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